

AMENDMENT AND RESPONSE UNDER 37 CFR § 1.111  
Serial Number: 09/643,128  
Filing Date: August 21, 2000  
Title: Gene Inactivation by targeted DNA methylation

Page 7  
Dkt: GMR-001

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**Amendments to the Claims:**

Please amend the claims as follows:

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (currently amended) A polynucleotide capable of inducing methylation at a target nucleotide sequence comprising:  
an oligonucleotide imprinting element, wherein said imprinting element is double stranded and has a first strand and a second strand complementary to said first strand, said first strand comprising at least one m5CG sequence paired with an unmethylated CG sequence on said second strand or at least one m5CN1G sequence paired with an unmethylated CN2G sequence on said second strand, wherein N1 is any nucleotide, and N2 is a nucleotide that pairs with N1; and  
a single stranded oligonucleotide guiding element comprising at least one m5CG or at least one m5CN3G sequence, wherein N3 is any nucleotide and said guiding element is complementary to a target nucleotide sequence; and  
wherein said imprinting element and said guiding element are operably linked to form a polynucleotide capable of inducing methylation at said target nucleotide sequence.
2. (original) The polynucleotide of claim 1 wherein said first strand and said second strand of said imprinting element are linked through a covalent linkage.
3. (original) The polynucleotide of claim 2 wherein said first strand and said second strand of said imprinting element are linked by one or more nucleotide residues.
4. (original) The polynucleotide of claim 3 wherein said first strand and said second strand of said imprinting element are linked by a single thymidine residue.

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Page 8  
Dkt: GMR-001

5. (original) The polynucleotide of claim 1 wherein said first strand of said imprinting element comprises at least two m5CG sequences, two m5CN1G sequences, or one m5CG sequence and one m5CN1G sequence.
6. (original) The polynucleotide of claim 5 wherein said first strand of said imprinting element comprises the sequence: 5'-m5CGpN1m5CG-3'.
7. (original) The polynucleotide of claim 6 wherein said first strand of said imprinting element comprises the sequence: 5'-m5CGpTpm5CG-3'.
8. (currently amended) The polynucleotide of claim 7 wherein said imprinting element comprises the sequence: 5'-CGpApCG-T-m5CGpTpm5CG-3' (SEQ ID NO: [[zz]] 1)
9. (original) The polynucleotide of claim 1 wherein said guiding element is about 15 to about 30 nucleotides in length.
10. (currently amended) The polynucleotide of claim 9 wherein said guiding element is a 22-nucleotide oligomer having the sequence 5'-AGCC<sup>m</sup>CGGG<sup>m</sup>CTGGGAGGAGT<sup>m</sup>CGG-3' (SEQ ID NO: [[zz]] 2).
11. (currently amended) The polynucleotide of claim 10 having the sequence 5'-CGACGT<sup>m</sup>CGpTp<sup>m</sup>CGAGCC<sup>m</sup>CGGG<sup>m</sup>CTGGGAGGAGT<sup>m</sup>CGG-3' (SEQ ID NO: [[zz]] 3).
12. (original) The polynucleotide of claim 1 wherein said guiding element is operably linked to the 3' end of said imprinting element.
13. (original) The polynucleotide of claim 1 wherein said target nucleotide sequence is in a gene.
14. (original) The polynucleotide of claim 13 wherein said target nucleotide sequence is in a gene regulatory region.
15. (original) The polynucleotide of claim 14 wherein said gene encodes a protein of unknown function.
16. (original) The polynucleotide of claim 15 wherein the gene is a disease gene.

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Page 9  
Dkt: GMR-001

17. (original) The polynucleotide of claim 16 wherein the disease is cancer.
18. (original) The polynucleotide of claim 14 wherein said target nucleotide sequence is in a gene regulatory region of human Igf2.
19. (original) A composition comprising the polynucleotide of claim 1 and one or more additional components.
20. (original) The composition of claim 19 wherein said additional component is one that facilitates entry of the polynucleotide into a cell.
21. (original) The composition of claim 20 wherein said additional component comprises one or more lipids.
22. (original) The composition of claim 21 wherein said one or more lipids comprise the cationic lipids N-[1-(2,3-dioleoyloxy)propyl]-n,n,n-trimethylammonium chloride (DOTMA), dioleoyl phosphatidylethanolamine (DOPE) and/or dioleoyl phosphatidylcholine (DOPC).
23. (original) The composition of claim 19 wherein said additional component is a physiologically acceptable carrier.
24. (original) A method for inducing methylation at a target nucleotide sequence in a cell comprising introducing the polynucleotide of claim 1 into a cell comprising said target nucleotide sequence, thereby inducing methylation at said target nucleotide sequence.
25. (original) The method of claim 24 wherein said cell is a mammalian cell, a plant cell, or a prokaryotic cell.
26. (original) The method of claim 25 wherein said cell is a human cell.
27. (original) The method of claim 24 wherein said polynucleotide is introduced into said cell *in vivo*.
28. (original) The method of claim 24 wherein said polynucleotide is introduced into said cell *ex vivo*.

## AMENDMENT AND RESPONSE UNDER 37 CFR § 1.111

Serial Number: 09/643,128

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Title: Gene Inactivation by targeted DNA methylation

Page 10  
Dkt: GMR-001

29. (original) The method of claim 24 wherein said polynucleotide is introduced as a composition comprising a lipid.
30. (original) The method of claim 24 additionally comprising determining a phenotypic change associated with methylation at said target nucleotide sequence after introduction of said polynucleotide.
31. (original) The method of claim 30 wherein said target nucleotide sequence is in a gene encoding a protein of unknown function.
32. (original) The method of claim 24 additionally comprising producing an organism from said cell, wherein said target sequence is in a gene, and the organism either does not express said gene or expresses said gene at a reduced level compared to a normal organism.
33. (original) The method of claim 24 wherein said target nucleotide sequence is in a disease gene.
34. (original) The method of claim 33 wherein said disease is cancer.

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CENTRAL FAX CENTER  
OCT 03 2006Page 11  
Dkt: GMR-001REMARKS

Applicant has carefully reviewed and considered the Sequence Error Report dated February 16, 2005. As instructed, the Sequence Listing has been amended following the Guidelines and checked with the CHECKER program. The enclosed printed sequence listing is the same as the enclosed computer-readable form.

In addition, the specification and claims have been amended to incorporate the sequence numbers and to delete the sequence numbers of 10 residues or less. All claims are repeated in the required format. There is no new matter.

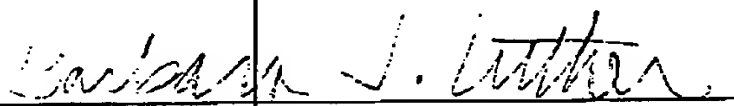
Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (480-344-7745) to facilitate prosecution of this application.

Respectfully submitted,

Date October 3, 2006

By

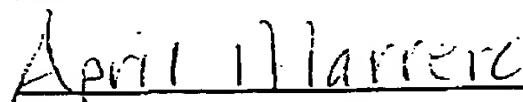


Barbara J. Luther

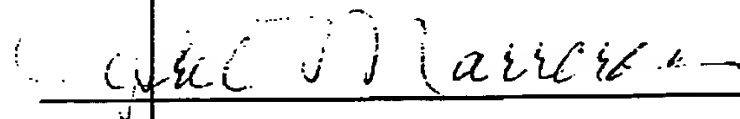
Reg. No. 33,954

The Luther Law Firm  
12198 East Columbine Dr.  
Scottsdale, AZ 85259  
Tel: 480-275-8302  
Fax: 480-275-8303  
Email: bjluther@cox.net

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is transmitted by facsimile to the USPTO general number 571-273-8300 on this 3d day of October, 2006.



Name



Signature